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TECHNICAL REPORT 9008

IV FLUIDMAKER II. TEST AND EVALUATION OF 6 L/HR PROTOTYPE

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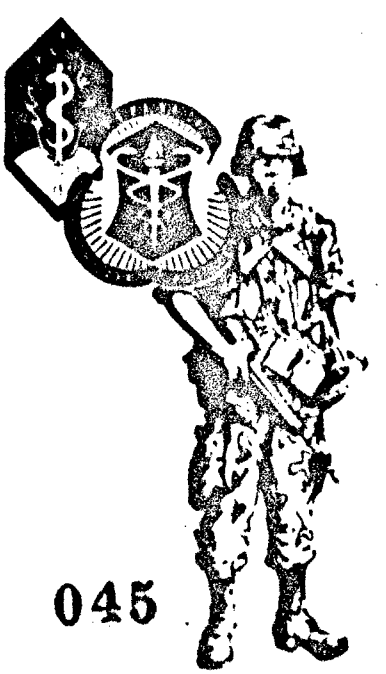
March 1991



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UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION: Unclassified

1b. RESTRICTIVE MARKINGS:

2a. SECURITY CLASSIFICATION AUTHORITY:

2b. DECLASSIFICATION/DOWNGRADING SCHEDULE:

3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution unlimited.

4. PERFORMING ORGANIZATION REPORT NUMBER(S): Technical Report No. 9008

5. MONITORING ORGANIZATION REPORT NUMBER(S):

6a. NAME OF PERFORMING ORGANIZATION: U.S. Army Biomedical Research and Development Laboratory

6b. OFFICE SYMBOL (If applicable): SGRD-UBE

7a. NAME OF MONITORING ORGANIZATION:

6c. ADDRESS (City, State, and ZIP Code): Fort Detrick, Frederick, Maryland 21702-5010

7b. ADDRESS (City, State, and ZIP Code):

8a. NAME OF FUNDING/SPONSORING ORGANIZATION:

8b. OFFICE SYMBOL (If applicable):

9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER:

8c. ADDRESS (City, State, and ZIP Code):

10. SOURCE OF FUNDING NUMBERS

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
62787A	3S162787B 874	8741KA	742 DA313646

11. TITLE (Include Security Classification): IV FLUIDMAKER II. TEST AND EVALUATION OF 6 L/HR PROTOTYPE

12. PERSONAL AUTHOR(S): T. Lynn Rogers, Jr., W. Dickinson Burrows, and James H. Nelson

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Technical Report	FROM 90-01-01 TO 91-03-29	March 1991	21

16. SUPPLEMENTARY NOTATION:

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Water for injection; Pyrogen-free water; Sterile water; Filtration; Reverse osmosis; Ion exchange; Carbon adsorption
06	12		

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Five hand-operated intravenous (iv) fluidmakers capable of producing 6 L/hr of water for injection have been tested for endotoxin, oxidizables and chloride content and sterility of product water from a challenge water having high levels of all measured parameters. Three of the fluidmakers incorporated a reverse osmosis unit, ion exchange column, water purification filter and sterilizing filter in series; the remaining two lacked the ion exchange column, but were otherwise identical. Fifty 1.0-L samples were produced with each fluidmaker. All samples were sterile and all but one were within the limit for pyrogenicity; 8 percent were out of limit for oxidizables and nearly all were out of limit for chloride ion. Further testing for removal of oxidizables and development of a suitable ion exchange unit are recommended.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT: ☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT ☐ DTIC USERS

21. ABSTRACT SECURITY CLASSIFICATION: Unclassified

22a. NAME OF RESPONSIBLE INDIVIDUAL: James H. Nelson

22b. TELEPHONE (Include Area Code): 301/663-7277

22c. OFFICE SYMBOL: SGRD-UBE

DD Form 1473, JUN 86 — Previous editions are obsolete.

SECURITY CLASSIFICATION OF THIS PAGE
UNCLASSIFIED

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PREFACE

Chemical analyses were performed under the direction of Dr. Steven H. Hoke, U.S. Army Biomedical Research and Development Laboratory (USABRDL). Pyrogen tests were conducted by Ms. Kathleen Connor of Program Resources, Incorporated. Sterile water tests were carried out under the direction of Ms. Linda Speights, U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). USABRDL acknowledges with gratitude the assistance of the following Medical Research Volunteers from USAMRIID: PFC John West, SPC Paul Gilson, PFC Grant Wright and SPC Peter Tebo.

INTRODUCTION

The U.S. Army Medical Research and Development Command requires a device to manufacture intravenous (iv) fluids in adverse circumstances, such as a field combat situation, where resupply of medical items is uncertain.[1] The device must produce sterile, pyrogen-free water which can be introduced directly into sterile bags with sterile admixtures to make one liter of Ringer's lactate or 1.0 L of 5 percent dextrose in water suitable for iv infusion into humans. Approval by the Food and Drug Administration (FDA) will ultimately be required, but is not considered to be a part of this effort. Salient requirements for the device are:

a. It must be hand-operated.

b. It must produce at least 1.0 L/hr of fluid.

c. The supply water must be taken from a potable source.

d. It should fit into a protective mask container (ca 20 cm X 23 cm X 8 cm).

In a previous study, two systems were devised for generating sterile, pyrogen-free water for injection (WFI) and were shown capable of producing WFI according to U.S. Pharmacopeia (USP) standards while meeting the other design requirements presented above.[2] Both systems utilize reverse osmosis (RO), ion exchange, a solid matrix filter containing activated carbon and zeta adsorbent, a final 0.2 μm pore-size sterilizing filter and a device for transferring the WFI to an iv bag. The smaller system weighs approximately 1.5 kg and produces WFI at a rate of 1.0 L in 45-50 min; the larger (which somewhat exceeds the desired size) weighs approximately 3.5 kg and produces 1.0 L of WFI in 5-6 min.

The present study was undertaken to evaluate the performance and reliability of each system under conditions more nearly approaching field utilization. This report presents results and conclusions from tests using the larger unit; results from tests using the smaller unit will be addressed in a subsequent report.

APPROACH AND RATIONALE

General performance requirements for the fluidmaker in terms of product quality are that it reduce dissolved inorganic and organic chemicals, including pyrogens, to very low levels; that it virtually eliminate residual suspended materials; and that it assure sterile transfer to an iv bag. The target for the device in question (hereinafter the fluidmaker) is Sterile WFI as defined by the USPXXII. The USP manufacturing and purity criteria for Sterile Water for Injection are presented in Appendix A.

For purification dechlorinated water passes sequentially through a reverse osmosis membrane, mixed-bed ion exchange resin, an activated carbon filter and

a sterilizing filter. The reverse osmosis membrane excludes all common ions and heavy metals by 98 percent or greater and effectively removes most dissolved organic impurities and all microorganisms, including viruses. The mixed-bed ion exchange column reduces dissolved salts to levels acceptable for WFI. A water purification filter containing activated carbon then traps organic chemicals missed by RO and removes pathogens and pyrogens. A membrane filter of 0.2 μm limiting pore size follows the water purification filter to ensure sterility. The product WFI is transferred through a closed system to an iv bag. Except as noted below, system components were identical with those described in the original study[2].

Because USABRDL in-house resources were insufficient to perform the entire battery of tests required by USPXXII, tests were limited to the following: endotoxins, sterility, total chloride, pH and oxidizable substances. Limited heavy metal analyses were also performed. It is believed that evaluation of these parameters provides an adequate test of each component of the fluidmaker.

MATERIALS AND METHODS

REVERSE OSMOSIS. The Survivor™ 35 (S35) hand-operated RO unit (Recovery Engineering, Inc., Minneapolis, MN) was used for all tests. Although the S35 has a lower production rate than the Survivor™ A90 used in the earlier studies (6 L/hr vs 10 L/hr) and is the same size, we chose the S35 on the recommendation of the manufacturer because it is more readily available, more easily maintained, and costs about $300 per unit less. Unlike the A90, the S35 cannot be disassembled for storage. Five RO units were used in this test.

ION EXCHANGE COLUMN. The smallest ion exchange (IE) columns available off-the-shelf were purchased from Vaponics, Inc., Plymouth, MA (Cat. No. MRN-254F). Ten inches long, the IE columns were packed with strong acid - strong base mixed bed ion exchange resin and were fitted with end cap nipples. These units were much larger than necessary for a field device, but were used because of their availability. These IE columns were connected to the outlet port of three of the five RO units. Inlet and outlet nipples were fitted with Luer-lok® connectors. The IE column was attached to the RO unit by Tygon® tubing.

WATER PURIFICATION FILTER. The First Need® water purification filter (General Ecology, Inc., Lionville, PA) used throughout this study is a solid matrix filter containing activated carbon and zeta adsorbents; it is rated at 0.1 μm nominal and 0.4 μm absolute pore size. It is a cylinder 7 cm in diameter, ca. 10 cm long, weighs 0.20 kg, and produces 400 to 500 mL/min at the maximum pumping rate recommended by the manufacturer. Holdup is 20 to 30 mL. Inlet and outlet nipples were fitted with Luer-Lok® connectors. The water purification filter was attached to the IE column or directly to the RO unit by Tygon® tubing. Although this filter provided sterile water in tests conducted by USABRDL,[2] it is not irradiated, autoclaved or otherwise sterilized during manufacture, and cannot be assumed to provide a consistently sterile product.

STERILIZING FILTER. Cameo IV presterilized syringe filters utilized a nylon membrane with a 0.2 μm pore size (Micron Separations Inc., Westborough, MA, Cat. No. DDN-0200S-15) and were rated at 100 mL/min. They were attached directly to First Need[R] filters by Luer-Lok[R] connectors and replaced as necessary (Appendix C). Product water was collected from the end of the sterilizing filter into sterile sample vials, but without benefit of a sterile transfer procedure. This collection procedure was necessitated by the unavailability of enough sterile transfer sets, as used in the original study,[2] but did not appear to affect product water quality adversely.

SAMPLING AND TESTING PROCEDURE. Challenge water (450 gal) was prepared by amending Fort Detrick tap water with sodium chloride (820 mg/L) and t-butyl alcohol. The water was dechlorinated by stirring for several days. The t-butyl alcohol was added in three aliquots of 170 g (100 mg/L) each on February 5, 12 and 20. Analyses of challenge water are presented in Appendix B. By the end of the test period, the supply water was visibly dirty and appeared contaminated with algae. Samples were collected for each liter of product water according to the schedule in Appendix C and tested for endotoxin, chloride, oxidizables, and sterility. First Need[R] filters and sterilizing filters were replaced at the beginning of each work day and after work breaks. Sterilizing filters were also replaced when they became plugged with particulate matter from the First Need[R] filters.

ANALYTICAL PROCEDURES. Pyrogen content was determined using the Limulus amebocyte lysate (LAL) chromogenic assay. Sterility of water samples was tested by plating 1.0 mL (diluted as necessary with sterile water) on sheep's blood agar and MacConkey's agar. Chloride ion concentration was determined by ion chromatography. Oxidizable substances were determined by the USP procedure (Appendix A). The detection limit for t-butyl alcohol as an oxidizable substance was 60 mg/L.

RESULTS AND DISCUSSION

Fifty 1.0 L samples of product water were collected from each of the five fluidmakers. Analytical results are summarized in Table 1. Integrity of product water with respect to sterility was complete. Although the challenge level far exceeded that of any likely potable source, no growth was detected for any sample on either sheep's blood agar or MacConkey's agar. Endotoxin levels were below the USPXXII limit and were generally below the detection limit for all but one sample. Again, the challenge level far exceeded that of any likely potable source. The endotoxin level of the single out-of-limit sample, 7.67 eu/mL (Appendix Table C4), was so high as to suggest external contamination or analytical error. These tests demonstrate that the fluidmaker reliably produces sterile, pyrogen free water.

Concerning oxidizable substances, 8 percent of the samples were out of limit. It is notable that in virtually every case out-of-limit samples followed installation of a new First Need[R] filter. This is consistent with the common observation that many grades of activated carbon release organic materials (phenolics, among others) when first put into service for water treatment. In retrospect, t-butyl alcohol may not have been the most

appropriate challenge. On the one hand, it is a type of material not commonly found in potable water except as a contaminant at levels far below the challenge level, and not readily removed by activated carbon or reverse osmosis. On the other hand, the detection limit is high by the method of USPXXII. These results suggest that further testing should be performed using a more realistic challenge, and that a random selection of First Need[R] filters should be tested for release of oxidizables.

Chloride ion levels in product water were out of limit for nearly every sample, commonly by a factor of two or more, whether or not an ion exchange column was installed. The chloride level of the challenge water matched that to be expected for potable water produced by the Army's reverse osmosis water purification unit (ROWPU) when drawing its supply from seawater. These results indicate that a different ion exchange unit will be needed to meet the chloride standard of USPXXII. This Laboratory is presently developing such a device under contract. Of interest is the fact that the fluidmaker produces a pulse of chloride ion in the first few liters after the unit has been idle for 24 hours or more, whether or not an ion exchange unit is installed (Figure 1, page 6). This is consistent with the observations of others, and has important implications concerning the final configuration of the fluidmaker.

TABLE 1. SUMMARY OF TEST RESULTS

Unit no.	Endotoxins		Sterility		Oxidizables		Chloride	
	total[a]	o/l[b]	total	o/l	total	o/l	total	o/l
1 (IE)[c]	50	0	50	0	50	3	50	49
2 (IE)	50	0	50	0	50	6	50	49
3 (IE)	50	0	50	0	50	4	50	49
4	50	1	50	0	50	3	50	50
5	50	0	50	0	49	4	49	49

a. Total number of 1.0 L samples
b. o/l = out of limit
c. These units included an ion exchange column.

The fluidmaker system functioned flawlessly from a mechanical standpoint with one important exception. Sterilizing filters were frequently plugged by particulate material from the First Need[R] filters, a problem not encountered during the bench-scale development program (2). This may not be a problem in actual field use, since it will probably be recommended that the sterilizing filter be part of the transfer set and be replaced with each liter of product. Discussion with the manufacturer of the First Need[R] filter revealed that discharge of traces of fine carbon particles is characteristic of this device,

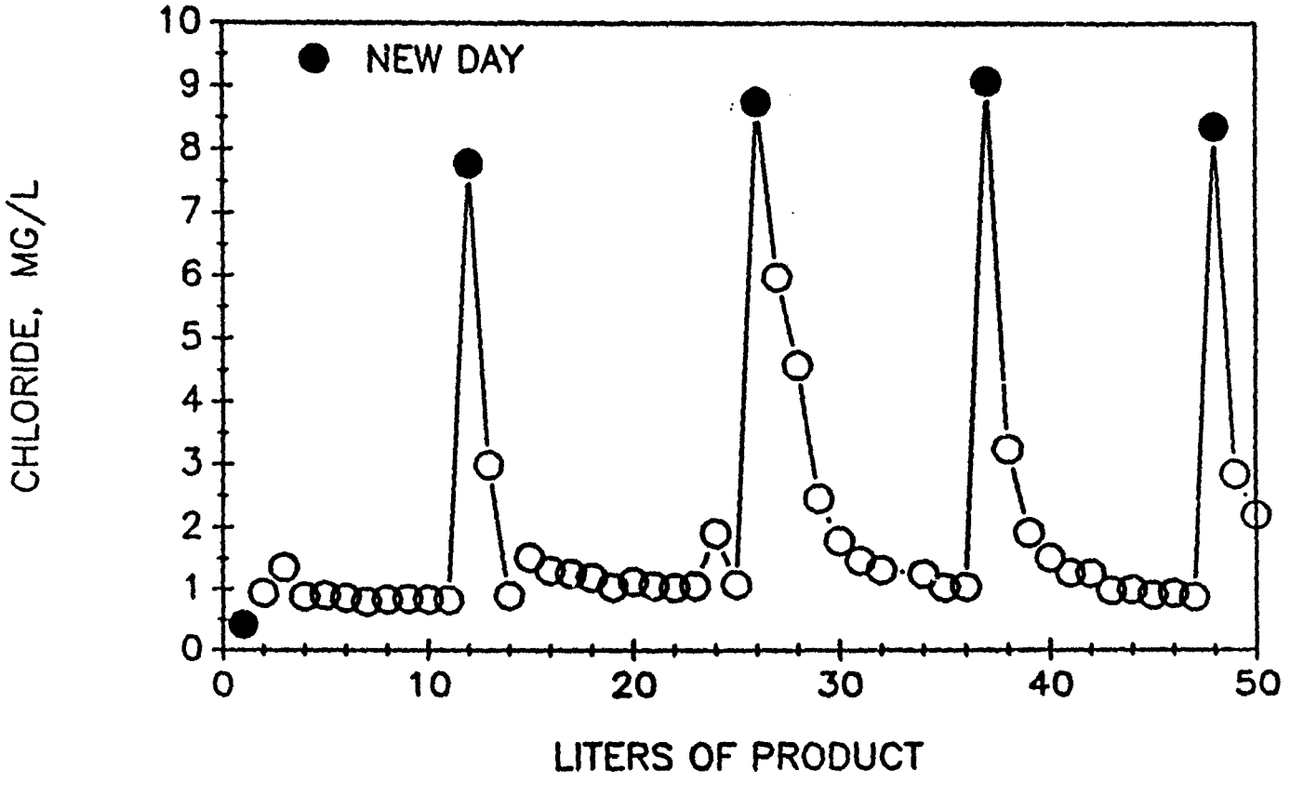

Figure 1. Effect of Idle Time on Chloride Content of Product Water (Unit No. 3)

at least for the first few liters of product. Development of a small, inline prefilter (depth filter) would address this problem. An alternative would be to wash the carbon filter with several liters of WFI during manufacture; this would have the additional virtue of removing the releasable organics believed to cause initial out-of-limit tests for oxidizables.

SUMMARY AND RECOMMENDATIONS

1. The 6 L/hr fluidmaker tested is a mechanically robust device which reliably produces sterile, pyrogen-free water from microbiologically contaminated potable water.

2. Further testing is needed to establish whether this device can meet the limit for oxidizable substances of USPXXII from a realistic challenge water. For this purpose, only the First Need^{R} filter requires testing.

3. An ion exchange unit specifically designed for this system is needed. No further action is required at this time, since contracts to address this problem are in effect.

4. It may be necessary to develop a small, inline prefilter (depth filter) to protect the final sterilizing filter from fine particulates shed by the First Need^{R} filter. An alternative would be to correct the problem during manufacture by washing the filter with WFI.

LITERATURE CITED

1. Memorandum, US Army Medical Research and Development Command, SGRD-PLB, 21 April 1988, subject: IV Fluidmaker.

2. Burrows, W.D., and J.H. Nelson. 1988. IV Fluidmaker: Preparation of Sterile Water for Injection in a Field Setting. Technical Report 8814, AD A207411, U.S. Army Biomedical Research and Development Laboratory, Fort Detrick, Frederick, MD.

3. The United States Pharmacopeia, Twenty-Second Revision. 1990. United States Pharmacopeial Convention, Inc., Rockville, MD.

APPENDIX A: STERILE WATER FOR INJECTION[3]

Sterile Water for Injection is Water for Injection sterilized and suitably packaged. It contains no antimicrobial agent or other added substance.

Packaging and storage -- Preserve in single-dose containers, preferably of Type I or Type II glass, of not larger than 1-liter size.
Labeling -- Label it to indicate that no antimicrobial or other substance has been added, and that it is not suitable for intravascular injection without its first having been made appropriately isotonic by the addition of a suitable solute.
Reference standard -- USP Endotoxin Reference Standard.
Bacterial endotoxins -- When tested as directed under Bacterial Endotoxins Test <85>, the USP Endotoxin RS being used, it contains not more than 0.25 USP Endotoxin Unit per mL.
Sterility -- It meets the requirements under Sterility Tests <71>.
Ammonia -- For Sterile Water for Injection in glass containers holding a volume up to 50 mL, dilute 50 mL with 50 mL of High-purity Water (see Reagents under Containers <661>), and use this dilution as the test solution; where larger volumes are held, use 100 mL of Sterile Water for Injection as the test solution. To 100 mL of the test solution add 2 mL of mercuric-potassium iodide TS: any yellow color produced immediately is not darker than that of a control containing 30 µg of added NH_3 in High-purity Water (see Reagents under Containers <661>)(0.6 ppm for Sterile Water for Injection packaged in volumes up to 50 mL in containers; 0.3 ppm for larger volumes).
Chloride -- To 20 mL in a color-comparison tube add 5 drops of nitric acid and 1 mL of silver nitrate TS, and gently mix: any turbidity formed within 10 minutes is not greater than that produced in a similarly treated control consisting of 20 mL of High-purity Water (see under Reagents in Containers <661>) containing 10 µg of Cl^- (0.5 ppm), viewed downward over a dark surface with light entering the tubes from the sides.
Oxidizable substances -- To 100 mL add 10 mL of 2 N sulfuric acid, and heat to boiling. For Sterile Water for Injection in containers holding a volume up to 50 mL, add 0.4 mL of 0.1 N potassium permanganate, and boil for 5 minutes; for larger volumes, add 0.2 mL of 0.1 N potassium permanganate, and boil for 5 minutes: the pink color does not completely disappear.
Total solids -- Proceed as directed in the test for Total solids under Purified Water. The following limits apply for Sterile Water for Injection in glass containers holding up to 30 mL, 0.004%; from 30 mL up to 100 mL, 0.003%; and for larger volumes, 0.002%.
Other requirements -- It meets the requirements of the tests for pH, Sulfate, Calcium, Carbon dioxide, and Heavy metals under Purified Water.

APPENDIX B: TEST WATER SUPPLY ANALYSES

Date	Pyrogen eu/mL[a]	Sterility cfu/mL[b]	Chloride mg/L	Oxidizables mg/L[c]	pH
02-05-90	18	3,000	577	>100	7
02-06-90	55.4	>100,000	541	>100	7
02-07-90	169.7	>100,000	531	>100	7
02-08-90	508.5	>100,000	646	>100	7
02-09-90	161.3	>100,000	591	>100	6
02-12-90	466.1	>100,000	684	>100	7
02-13-90	743.6	>100,000	587	>100	7
02-14-90	554.3	>100,000	542	>100	7
02-15-90	270	>100,000	558	>100	7
02-16-90	893.3	>100,000	549	>100	7
02-20-90	1,128.3	75,000	544	>100	7
02-21-90	900	d	567	>100	7
02-22-90	864.1	>100,000	602	>100	7

a. Endotoxin units/mL
b. Colony-forming units/mL
c. As t-butyl alcohol
d. Limited growth on either MacConkey's agar or sheep's blood agar

APPENDIX C: TEST RESULTS

TABLE C1. TEST UNIT NO. 1: WITH ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen eu/ml[a]	Sterility cfu/ml[b]	Chloride mg/L	Oxidiz.
		carbon	steril.				
02-05-90	1002	new	new	<0.06	0	1.921	+
	1007			0.07	0	0.243	+
	1012			0.07	0	1.252	-
	1017			<0.06	0	0.902	-
	1022			<0.06	0	0.884	-
	1027			<0.06	0	1.248	-
	1032			<0.06	0	0.967	-
	1037		new	<0.06	0	0.814	-
	1042			<0.06	0	0.847	-
	1047			<0.06	0	1.026	-
	1052			<0.06	0	0.925	-
	1057			<0.06	0	0.919	-
	1062			<0.06	0	1.040	-
	1067			<0.06	0	0.962	-
	1072			<0.06	0	1.024	-
	1077			<0.06	0	0.990	-
	1082			<0.06	0	0.895	-
	1087			<0.06	0	0.960	-
02-06-90	1092	new	new	<0.06	0	6.430	+
	1097			<0.06	0	2.821	-
	1102			<0.06	0	2.054	-
	1107			<0.06	0	1.632	-
	1112			<0.06	0	1.490	-
	1117			<0.06	0	1.310	-
	1122			<0.06	0	1.283	-
	1257	new	new	<0.06	0	2.141	-
	1262			<0.06	0	1.428	-
	1267			<0.06	0	1.170	-
	1272			<0.06	0	1.052	-
	1277			<0.06	0	1.006	-
	1282			<0.06	0	0.954	-
	1287			<0.06	0	0.887	-
	1292		new	<0.06	0	0.940	-
	1297			<0.06	0	0.774	-
	1302			<0.06	0	0.808	-
	1307			<0.06	0	0.760	-
	1312			<0.06	0	0.890	-
02-15-90	1317	new	new	<0.06	0	5.220	-
	1322			<0.06	0	2.287	-
	1327			<0.06	0	1.443	-
	1332			<0.06	0	1.106	-
	1337			<0.06	0	1.011	-
	1342			<0.06	0	0.914	-

TABLE C1. TEST UNIT NO. 1: WITH ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen	Sterility	Chloride	Oxidiz.
		carbon	steril.	eu/ml[a]	cfu/ml[b]	mg/L	
	1347		new	<0.06	0	0.885	-
	1352			<0.06	0	0.861	-
	1357			<0.06	0	0.898	-
	1362			<0.06	0	0.837	-
	1367			<0.06	0	0.846	-
	1372			<0.06	0	0.851	-
	1377			0.18	0	2.000	-

a. Endotoxin units
b. Colony-forming units; 0 = no growth in 48 hours

TABLE C2. TEST UNIT NO. 2: WITH ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen	Sterility	Chloride	Oxidiz.
		carbon	steril.	eu/ml[a]	cfu/ml[b]	mg/L	
02-05-90	1003	new	new	<0.06	0	0.311	+
	1008			<0.06	0	0.762	+
	1013			<0.06	0	1.987	+
	1018			<0.06	0	0.991	+
	1023		new	<0.06	0	0.938	+
	1028			<0.06	0	1.103	-
	1033			<0.06	0	1.011	-
	1038			<0.06	0	1.037	-
	1043			<0.06	0	1.005	-
	1048			<0.06	0	1.204	-
	1053			<0.06	0	0.866	-
	1058			<0.06	0	0.957	-
	1063			0.12	0	1.652	-
	1068		new	<0.06	0	0.960	-
	1073			<0.06	0	0.925	-
	1078			<0.06	0	10.035	+
	1083			<0.06	0	0.944	-
	1088			<0.06	0	3.399	-
	1093			<0.06	0	2.356	-
	1098			<0.06	0	1.620	-
	1103			<0.06	0	1.503	-
	1108			<0.06	0	1.516	-
	1113			<0.06	0	1.283	-
	1123			<0.06	0	1.018	-
	1258		new	<0.06	0	3.871	-

TABLE C2. TEST UNIT NO. 2: WITH ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen	Sterility	Chloride	Oxidiz.
		carbon	steril.	eu/ml[a]	cfu/ml[b]	mg/L	
	1263			<0.06	0	2.382	-
	1268			<0.06	0	2.267	-
02-15-90	1273	new	new	<0.06	0	16.605	-
	1278			<0.06	0	5.919	-
	1283			<0.06	0	4.457	-
	1288			<0.06	0	4.589	-
	1293			<0.06	0	3.760	-
	1298			<0.06	0	3.458	-
	1303			<0.06	0	2.869	-
	1308			<0.06	0	3.085	-
	1313			<0.06	0	3.620	-
	1318		new	<0.06	0	2.886	-
	1323			<0.06	0	2.422	-
	1328			<0.06	0	2.421	-
	1333			<0.06	0	2.465	-
	1338			<0.06	0	2.142	-
02-16-90	1343	new	new	<0.06	0	23.295	-
	1348			<0.06	0	8.554	-
	1353			<0.06	0	5.745	-
	1358			<0.06	0	4.409	-
	1363		new	<0.06	0	4.018	-
	1368			<0.06	0	5.325	-
	1373			<0.06	0	3.897	-
	1378			<0.06	0	3.524	-

a. Endotoxin units
b. Colony-forming units; 0 = no growth in 48 hours

TABLE C3. TEST UNIT NO. 3: WITH ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen	Sterility	Chloride	Oxidiz.
		carbon	steril.	eu/ml[a]	cfu/ml[b]	mg/L	
02-05-90	1004	new	new	<0.06	0	0.420	+
	1009			0.15	0	0.939	+
	1014			0.07	0	1.368	-
	1019			<0.06	0	0.880	+
	1024			<0.06	0	0.901	-
	1029			<0.06	0	0.863	-
	1034			<0.06	0	0.799	-
	1039			<0.06	0	0.835	-

TABLE C3. TEST UNIT NO. 3: WITH ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen	Steri ity	Chloride	Oxidiz.
		carbon	steril.	eu/ml[a]	cfu/ml[b]	mg/L	
	1044			<0.06	0	0.849	-
	1049			<0.06	0	0.837	-
	1054			<0.06	0	0.829	-
02-06-90	1059	new	new	<0.06	0	7.772	-
	1064			<0.06	0	2.990	-
	1069			<0.06	0	0.900	-
	1074			<0.06	0	1.518	-
	1079			<0.06	0	1.310	-
	1084			<0.06	0	1.259	-
	1089			<0.06	0	1.195	-
	1094			<0.06	0	1.039	-
	1099			<0.06	0	1.128	-
	1104			<0.06	0	1.062	-
	1109			<0.06	0	1.030	-
	1114			<0.06	0	1.059	-
	1119			<0.06	0	1.911	-
	1124			<0.06	0	1.082	-
02-20-90	1259	new	new	0.07	0	8.744	-
	1264			<0.06	0	5.967	+
	1269			<0.06	0	4.570	-
	1274			<0.06	0	2.465	-
	1279			<0.06	0	1.790	-
	1284			<0.06	0	1.474	-
	1289		new	<0.06	0	1.325	-
	1294			0.11	0	7.745[c]	-
	1299			<0.06	0	1.256	-
	1304			<0.06	0	1.034	-
	1309			0.11	0	1.045	-
02-21-90	1314	new	new	<0.06	0	9.075	-
	1319			<0.06	0	3.242	-
	1324			<0.06	0	1.922	-
	1329			<0.06	0	1.516	-
	1334			<0.06	0	1.272	-
	1339			<0.06	0	1.260	-
	1344		new	<0.06	0	0.982	-
	1349			<0.06	0	0.996	-
	1354		new	<0.06	0	0.907	-
	1359			<0.06	0	0.936	-
	1364			<0.06	0	0.878	-
02-22-90	1369	new	new	<0.06	0	8.352	-
	1374			<0.06	0	2.852	-
	1379			<0.06	0	2.204	-

a. Endotoxin units; b. Colony-forming units: 0 = no growth in 48 hours;
c. Value not included in Figure 1

TABLE C4. TEST UNIT NO. 4: WITHOUT ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen eu/ml[a]	Sterility cfu/ml[b]	Chloride mg/L	Oxidiz.
		carbon	steril.				
02-05-90	1005	new	new	<0.06	0	4.541	-
	1010			0.07	0	4.393	+
	1015			0.07	0	2.502	+
	1020			<0.06	0	2.225	-
	1025			<0.06	0	2.346	-
	1030			<0.06	0	3.750	-
	1035			<0.06	0	3.241	-
	1040			<0.06	0	4.590	-
	1045			<0.06	0	7.493	-
	1050			0.14	0	5.952	-
	1055		new	<0.06	0	5.633	-
02-06-90	1060	new	new	<0.06	0	27.812	+
	1065			<0.06	0	6.901	-
	1070			<0.06	0	3.613	-
	1075			<0.06	0	4.024	-
	1080			<0.06	0	3.976	-
	1085			<0.06	0	3.251	-
	1090			<0.06	0	3.509	-
	1095			<0.06	0	3.500	-
	1100			<0.06	0	3.970	-
	1105			<0.06	0	1.960	-
	1110			<0.06	0	3.417	-
	1115			<0.06	0	4.568	-
	1120			<0.06	0	2.444	-
	1125			<0.06	0	2.923	-
02-20-90	1260	new	new	0.14	0	9.096	-
	1265			<0.06	0	4.560	-
	1270			<0.06	0	2.905	-
	1275			<0.06	0	2.556	-
	1280			<0.06	0	2.054	-
	1285			<0.06	0	1.649	-
	1290			<0.06	0	1.696	-
	1295		new	7.67	0	1.584	-
	1300			0.11	0	1.912	-
	1305			0.15	0	1.849	-
	1310			<0.06	0	1.975	-
	1315			0.11	0	1.773	-
	1320			0.16	0	1.810	-
02-22-90	1325	new	new	0.07	0	15.370	-
	1330			<0.06	0	7.368	-
	1335			0.08	0	4.822	-
	1340			<0.06	0	4.384	-
	1345			<0.06	0	4.006	-
	1350			<0.06	0	3.761	-
	1355			0.21	0	4.524	-

TABLE C4. TEST UNIT NO. 4: WITHOUT ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen eu/ml[a]	Sterility cfu/ml[b]	Chloride mg/L	Oxidiz.
		carbon	steril.				
	1360			<0.06	0	4.703	-
	1365			<0.06	0	3.962	-
	1370			<0.06	0	4.007	-
	1375			<0.06	0	1.857	-
	1380			<0.06	0	2.312	-

a. Endotoxin units
b. Colony-forming units; 0 = no growth in 48 hours

TABLE C5. TEST UNIT NO. 5: WITHOUT ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen eu/ml[a]	Sterility cfu/ml[b]	Chloride mg/L	Oxidiz.
		carbon	steril.				
02-05-90	1006	new	new	<0.06	0	5.444	+
	1011			<0.06	0	4.209	+
	1016			<0.06	0	0.256	+
	1021			<0.06	0	3.303	-
	1026		new	<0.06	0	3.929	-
	1031			<0.06	0	4.324	-
	1036			<0.06	0	3.238	-
	1041			<0.06	0	4.053	-
	1046			<0.06	0	4.152	-
	1051		new	<0.06	0	3.847	-
	1056			<0.06	0	3.952	-
	1061			<0.06	0	3.570	-
	1066		new	<0.06	0	10.306	-
	1071			<0.06	0	8.858	-
	1076			<0.06	0	3.838	-
	1081			<0.06	0	3.504	-
	1086			<0.06	0	3.105	-
	1091			0.10	0	2.888	-
	1096			<0.06	0	3.088	-
	1101			<0.06	0	3.029	-
	1106			0.11	0	3.489	-
	1111			<0.06	0	3.201	-
	1116			<0.06	0	3.493	-
	1121			0.10	0	3.401	-
	1126			0.11	0	2.269	-
02-15-90	1261	new	new	0.09	0		
	1266		new	<0.06	0	9.831	+

TABLE C5. TEST UNIT NO. 5: WITHOUT ION EXCHANGE COLUMN

Date	Sample	Filters		Pyrogen	Sterility	Chloride	Oxidiz.
		carbon	steril.	eu/ml[a]	cfu/ml[b]	mg/L	
	1271			<0.06	0	3.001	-
	1276			<0.06	0	1.782	-
02-16-90	1281	new	new	<0.06	0	5.545	-
	1286			<0.06	0	3.486	-
	1291			<0.06	0	2.798	-
	1296			<0.06	0	2.343	-
	1301			<0.06	0	1.727	-
	1306			<0.06	0	1.474	-
	1311			<0.06	0	1.436	-
	1316			<0.06	0	1.197	-
02-20-90	1321	new	new	<0.06	0	7.249	-
	1326			<0.06	0	2.951	-
	1331			<0.06	0	1.764	-
	1336			0.07	0	1.610	-
	1341			0.13	0	1.286	-
	1346			0.13	0	1.124	-
	1351			0.13	0	1.006	-
	1356		new	<0.06	0	0.909	-
	1361			0.13	0	0.973	-
	1366			0.11	0	0.987	-
	1371			0.11	0	0.829	-
	1376			0.11	0	0.832	-
	1381			<0.06	0	0.858	-

a. Endotoxin units
b. Colony-forming units; 0 = no growth in 48 hours

APPENDIX D

GLOSSARY OF TERMS

USABRDL	U.S. Army Biomedical Research and Development Laboratory
cfu	colony forming units
eu	endotoxin units
FDA	U.S. Food and Drug Administration
IE	ion exchange
iv	intravenous
RO	reverse osmosis
ROWPU	Reverse Osmosis Water Purification Unit
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USP	U.S. Pharmacopeia
USPXXII	U.S. Pharmacopeia, Twenty-Second Revision

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